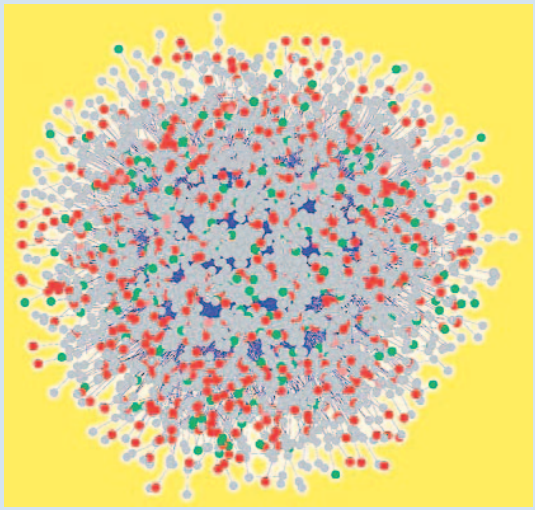
Metabolic Profiling:
Application to Toxicology and Risk Reduction

The NIEHS, with the NIH Office of Rare Diseases, the U.S. Food and Drug Administration, Paradigm Genetics, and Waters Corporation, cosponsored an international conference titled Metabolic Profiling: Application to Toxicology and Risk Reduction. The meeting, held 14–15 May 2003 in Research Triangle Park, North Carolina, convened a multidisciplinary group of research and computational scientists from academia, industry, and government to define the state of the science for the emerging area of metabolic profiling—also called metabonomics or metabolomics—and its application in basic and applied health research. A summary of the science of metabolic profiling as well as future research directions and challenges are summarized here. A full meeting report will be published later this year.



Metabolites are the end products of cellular processes, and their levels reflect the integrated response of biological systems to genetic and environmental influences. Metabolic profiling is defined as a high-throughput approach to measuring and interpreting the complex, time-related concentration, activity, and flux of endogenous metabolites in biosamples (urine, blood, tissues, cells).

Metabolomics is a new word but not a new science. Studies aimed at measuring metabolites in biological systems have been ongoing for more than 50 years, and there is a long history of studies on intermediary metabolism. What is new is the ability to measure and quantify the full complement of metabolites in a biosample, which greatly enhances our capability for scientific discovery. Integration of old and new studies is needed.

The metabolome is an integral part of biological pathways and networks that is "downstream" of the genome and the proteome. Consequently, the metabolome is more directly influenced by external agents such as diet, drugs, disease, and chemicals than either the genome or the proteome. Integrated studies involving these complementary data sets are needed to construct models of how biological pathways, networks, and systems function in producing toxicity and delivering health. This challenging task will require new databases and computational tools.

The metabolome is complex, involving a range of small molecules (peptides, lipids, amino acids) with varying size, structure, polarity, and function. There are several metabolic profiling technologies in use, including LC-MS/MS, NMR, and FT-MS. More work is needed to evaluate and improve the sensitivity and specificity of these technologies for a variety of applications (blood, urine, cells, cellular compartments).

There are ongoing efforts to link changes in metabolite profiles to histological changes in target organs and tissues. These studies should be expanded to include multiple time points and species, and to address normal variations in metabolites. This will allow validation of the use of metabolic profiling in predictive toxicology and risk assessment. Specific emphasis should be placed on describing the dynamics of metabolite activity and flux in biological systems.

Metabolic profiling approaches are being applied to drug development, detection of adverse responses, and disease diagnosis. Defining metabolite profiles in blood and urine samples has been used to classify the status and progression of metabolic disorders, diabetes, and neurodegenerative, renal, and cardiovascular diseases. Additional studies are needed to define the underlying biological mechanisms in order to personalize clinical diagnosis, treatment, and prevention.

The field of metabolic profiling offers tremendous opportunities for environmental health research; however, relatively little work has been devoted to environmental or occupational exposures. The NIEHS should take the lead and foster partnerships among federal agencies, academia, and industry to advance the application to toxicology and disease risk reduction.

Contact | **Brenda Weis, Ph.D., e-mail: weis@niehs.nih.gov**

For more information | **http://www.niehs.nih.gov/dert/metabol.htm**

Thomas J. Begley/Massachusetts Institute of Technology